

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
 United States Patent and Trademark
 Office
 Box PCT
 Washington, D.C.20231
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 16 May 2000 (16.05.00)	
International application No. PCT/GB99/03235	Applicant's or agent's file reference P21896A/RMC
International filing date (day/month/year) 30 September 1999 (30.09.99)	Priority date (day/month/year) 30 September 1998 (30.09.98)
Applicant McKEOWN, Stephanie et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

25 April 2000 (25.04.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Pascal Piriou Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

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From the INTERNATIONAL BUREAU

NOTICE INFORMING THE APPLICANT OF THE COMMUNICATION OF THE INTERNATIONAL APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

MURGITROYD & COMPANY

373 Scotland Street
Glasgow G5 8QA
ROYAUME-UN

MURGITROYD
& COMPANY

14 APR 2000

COMP RMC

Date of mailing (day/month/year) 06 April 2000 (06.04.00)		IMPORTANT NOTICE	
Applicant's or agent's file reference P21896A/RMC			
International application No. PCT/GB99/03235	International filing date (day/month/year) 30 September 1999 (30.09.99)	Priority date (day/month/year) 30 September 1998 (30.09.98)	
Applicant UNIVERSITY OF ULSTER AT JORDANSTOWN et al			

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:
AU,CN,JP,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CR,CU,CZ,DE,DK,DM,EA,EE,EP,ES,FI,GB,GD,GE,
GH,GM,HR,HU,ID,IL,IN,IS,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MD,MG,MK,MN,MW,MX,NO,NZ,OA,
PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,UA,UG,UZ,VN,YU,ZA,ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on
06 April 2000 (06.04.00) under No. WO 00/19208

REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer J. Zahra Telephone No. (41-22) 338.83.38
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M-H

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference P21896A/RMC	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/GB 99/ 03235	International filing date (day/month/year) 30/09/1999	(Earliest) Priority Date (day/month/year) 30/09/1998
Applicant UNIVERSITY OF ULSTER AT JORDANSTOWN et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

EGFR 37 KDA FRAGMENT AS CANCER MARKER

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/GB 99/03235

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/68 G01N33/574

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 92 21771 A (TRITON DIAGNOSTICS INC) 10 December 1992 (1992-12-10) claim 1	1-12
A	US 4 933 294 A (WATERFIELD MICHAEL D ET AL) 12 June 1990 (1990-06-12) abstract claims	1-12

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

21 January 2000

Date of mailing of the international search report

31/01/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Pellegrini, P

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/GB 99/03235

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9221771	A	10-12-1992	AU 2178292 A	08-01-1993
			US 5674753 A	07-10-1997
			US 5344760 A	06-09-1994
US 4933294	A	12-06-1990	AT 97498 T	15-12-1993
			AU 3934085 A	09-08-1985
			DE 3587657 D	23-12-1993
			EP 0171407 A	19-02-1986
			EP 0491675 A	24-06-1992
			WO 8503357 A	01-08-1985
			JP 61501168 T	12-06-1986

PATENT COOPERATION TREATY

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REC'D 27 DEC 2000

WIPO

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P21896/RMC	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/GB99/03235	International filing date (day/month/year) 30/09/1999	Priority date (day/month/year) 30/09/1998
International Patent Classification (IPC) or national classification and IPC G01N33/68		
Applicant UNIVERSITY OF ULSTER AT JORDANSTOWN et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 6 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 25/04/2000	Date of completion of this report 20.12.2000
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Bradbrook, D Telephone No. +49 89 2399 7413



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/03235

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).):*

Description, pages:

1-12 as originally filed

Claims, No.:

1-12 with telefax of 04/12/2000

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB99/03235

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-3,6,7,10-12.

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☒ the claims, or said claims Nos. 1-3,6,7,10-12 are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	4,5,8,9
	No:	Claims	
Inventive step (IS)	Yes:	Claims	4,5,8,9
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	4,5,8,9

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB99/03235

No: Claims

2. Citations and explanations
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

s e separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB99/03235

1. The applicant's observations submitted with the amended claims have been considered in establishing this report.

Section III

2. Non-establishment of opinion

The present invention is based on the finding that a 37kDa fragment is detected using the Ab4 EGFR antibody in samples from patients having bladder cancer. The fragment appears not to have been identified as a bona fide fragment of EGFR: this supposition seems to be based on its binding to the anti-EGFR Ab4 antibody, but this alone is inconclusive. The specification shows no comparative analysis of samples with different antibodies for EGFR or other antigens and provides no information as to the specificity of the antibody. With respect to antibody cross-reactivity, it is insufficient to suggest that the antibody is specific for EGFR merely because the peptide sequence to which it binds has no homology with other human proteins: antibody binding is more than a simple function of the amino acid sequence of a polypeptide.

In the present case, the fragment is characterized only by its size and binding to Ab4, neither of which features is sufficient on its own to properly define the fragment of interest. Thus, in claims 1-3, 6, 7 and 10-12, the fragment is not properly defined so that the scope of said claims is wider than is justified by the description (Article 6 PCT).

Section V

3. Reference is made to the following documents:

D1: US-A-4 933 294 (Waterfield et al., 12.07.90);

D2: WO-A-92 21771 (Triton Diagnostics Inc.; 10.12.92).

4. D1 discloses a method of detecting abnormalities in mammalian growth by correlation with the presence of a truncated epidermal growth factor receptor having a portion of its amino terminus deleted. The deleted portion preferably

contains the growth factor binding domain and represents about 500 amino acid residues (see claims). The remaining fragment would not correspond to that of the present invention.

D2 discloses methods of diagnosing neoplastic disease, including bladder and prostate cancers, by detecting in a body fluid the ectodomain of EGFR, having a molecular weight of 90-115 kDa (claims 1 and 7).

5. Present claims 4, 5, 8 and 9 appear to be novel and inventive (Article 33(2) and (3) PCT), as none of the available prior art documents, taken either alone or in combination, discloses the fragment of the present invention as a marker for bladder cancer or prostate cancer.

Section VIII

6. The feature "A marker for bladder cancer ...", to which claim 1 is directed, is a functional feature and leaves the reader in doubt as to the exact nature of the subject-matter being claimed, thereby rendering the definition of the subject-matter of said claim unclear (Article 6 PCT).
7. Should the present application enter the national or regional phase, the Ab4 antibody may not be considered to have been sufficiently disclosed, as there appears to be no reference to a certificate of deposition or equivalent documentation for said antibody. Reference to a commercial supplier and catalogue number is insufficient to unambiguously identify the antibody.

1 **CLAIMS**

2

3 1. A marker for bladder cancer, prostate cancer or
4 urinary infection, the marker consisting a 37KDa
5 fragment of EGFR.

6

7 2. A method for the diagnosis of first presentation
8 or recurrence of bladder cancer, the method
9 consisting of the detection of a 37KDa fragment of
10 EGFR in a urine sample.

11

12 3. A method as claimed in claim 2 wherein the
13 presence of the 37KDa EGFR fragment is detected
14 using an antibody.

15

16 4. A method as claimed in claim 2 or claim 3 wherein
17 the presence of 37KDa EGFR fragment is detected
18 using antibody Ab4 EGFR available from Oncogene
19 Science, Inc.

20

21 5. The use of antibody Ab4 EGFR in a test to detect
22 the presence of 37KDa EGFR fragment in urine as a
23 diagnostic test for bladder cancer.

24

25 6. A method for the diagnosis of prostate cancer, the
26 method comprising the detection of a 37KDa
27 fragment of EGFR in a urine sample.

28

29 7. A method as claimed in claim 6 wherein the
30 presence of the 37KDa EGFR fragment is detected
31 using an antibody.

32

33 8. A method as claimed in claim 6 or claim 7 wherein
34 the presence of 37KDa EGFR fragment is detected
35 using antibody Ab4 EGFR available from Oncogene
36 Science, Inc.

- 1
2 9. The use of antibody Ab4 EGFR in a test to detect
3 the presence of 37KDa EGFR fragment in urine as a
4 diagnostic test for prostate cancer.
5
6 10. A method for the diagnosis of bladder cancer,
7 and/or prostate cancer and/or urinary infection,
8 the method comprising a test for the presence of a
9 37KDa fragment of EGFR in a urine sample.
10
11 11. A method as claimed in any of claims 2 to 4 and 7
12 to 10 in the form of a dip-stick test.
13
14 12. The use of antibodies to the 37KDa fragment of
15 EGFR in the diagnosis of urinary infection,
16 bladder cancer and prostate cancer.
17
18



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : G01N 33/68, 33/574	A1	(11) International Publication Number: WO 00/19208 (43) International Publication Date: 6 April 2000 (06.04.00)
(21) International Application Number: PCT/GB99/03235 (22) International Filing Date: 30 September 1999 (30.09.99) (30) Priority Data: 9821170.9 30 September 1998 (30.09.98) GB (71) Applicant (for all designated States except US): UNIVERSITY OF ULSTER AT JORDANSTOWN [GB/GB]; Newtownabbey, Co Antrim BT37 0QB (GB). (72) Inventors; and (75) Inventors/Applicants (for US only): McKEOWN, Stephanie [GB/GB]; 14 Tillyrusk Road, Dundrod, Crumlin BT29 4JA (GB). RITCHIE, Joan [GB/GB]; 2 Ardymagh Road, Ballynashree, Ballyclare BT39 9TJ (GB). (74) Agent: MURGITROYD & COMPANY; 373 Scotland Street, Glasgow G5 8QA (GB).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RQ, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>
(54) Title: EGFR 37 KDA FRAGMENT AS CANCER MARKER (57) Abstract <p>The present invention relates to the presence of a 37KDa epidermal growth factor receptor (EGFR) fragment in the urine of patients with transitional cell carcinoma of the bladder. The presence of the 37KDa EGFR fragment in urine can be ascertained using an antibody. The presence of the 37KDa EGFR fragment in the urine of patients can be a test for the presence of prostate cancer and can therefore be used as a general screen for health in the genitourinary area.</p>		

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
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CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

INTERNATIONAL SEARCH REPORT

International Application No

/GB 99/03235

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 G01N33/68 G01N33/574

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 92 21771 A (TRITON DIAGNOSTICS INC) 10 December 1992 (1992-12-10) claim 1	1-12
A	US 4 933 294 A (WATERFIELD MICHAEL D ET AL) 12 June 1990 (1990-06-12) abstract claims	1-12

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

- "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- "&" document member of the same patent family

Date of the actual completion of the international search

21 January 2000

Date of mailing of the international search report

31/01/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
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Authorized officer

Pellegrini, P

INTERNATIONAL SEARCH REPORT

Information on patent family members

Patent International Application No

PCT/GB 99/03235

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9221771 A	10-12-1992	AU 2178292 A	08-01-1993
		US 5674753 A	07-10-1997
		US 5344760 A	06-09-1994
US 4933294 A	12-06-1990	AT 97498 T	15-12-1993
		AU 3934085 A	09-08-1985
		DE 3587657 D	23-12-1993
		EP 0171407 A	19-02-1986
		EP 0491675 A	24-06-1992
		WO 8503357 A	01-08-1985
		JP 61501168 T	12-06-1986